REMARKS

Claims 4-9 and 13-18 are pending and have been examined on the merits. Claims 4, 13 and 16 have been amended hereinabove. Support for the amended claims can be found in the specification, page 9, lines 3-14 and figure 4B. No new matter has been added.

In this Final Office Action, the claims are rejected and objected to as follows:

A) Claims 4-9 stand rejected under 35 U.S.C. § 103(a) as being obvious over Root et al. (Journal of General Virology, 2000, hereinafter "Root") in view of Stewart et al. (Biochemistry, 1999, hereinafter "Stewart") and Heredia et al. (Journal of Acquired Immune Deficiency Syndrome, 2000, hereinafter "Heredia");

B) Claims 13 and 16 are objected to because of informalities; and

C) Claims 13-18 are rejected under 35 U.S.C. § 103(a) as being obvious over Root in view of Stewart and Heredia.

Applicants respectfully traverse.

Rejection of Claims 4-9 and 13-18 under 35 U.S.C. § 103(a)

Applicants wish to incorporate by reference the previously filed response and wish to add the following additional remarks.

As previously submitted, the presently claimed invention is directed to methods for inhibiting and for treating influenza virus replication and infection by administering an effective amount of resveratrol. This effective amount of resveratrol non-reversibly inhibits influenza virus replication (*e.g.*, from page 8 line 21, to page 9 line 14).

As described in the specification at page 8, resveratrol was added according to different treatment schedules in relation to various phases of the life cycle of the virus. Thus, as shown in Figure 3, the entry of the virus was not inhibited by the drug.

Further, the specification discloses that resveratrol inhibits the synthesis of late influenza virus haemoagglutinin and matrix protease rather than the expression of the early nucleocapside and polymerase protein (*e.g.*, specification page 10). Accordingly, resveratrol inhibits influenza virus replication.

As set forth in the previous response, Root describes the highly specific PKC inhibitor bisindolylmaleimide I.HCl and describes its effect on the influenza virus entry and replication. Root further describes that virus replication is inhibited in a dose dependent and reversible manner and the replication is blocked very early during the infection, apparently during virus endocytosis and uncoating. That is, upon removal of the drug, the virus can resume the infection of the cell. Additionally, Root discloses that "these results suggest that the activity of PKC is crucial for influenza virus entry, and may be target for future antiviral therapy" (*e.g.*, page 2698, end of left col. to beginning of right col.).

Thus, Root does not disclose a method for non-reversibly inhibit influenza virus replication. On the contrary, Root discloses a reversible inhibition occuring during endocytosis mediated by bisindolylmaleimide. As such, Root does not disclose, teach or even suggest the presently claimed methods of non-reversibly inhibiting influenza virus replication with the PKC inhibitor resveratrol.

In addition, far from being "a distinction without a difference", the claimed invention's departure from the reference's teaching confers a number of advantages. For

example the use of resveratrol affords the advantage of attacking the virus indirectly, i.e. by interfering with a functional cell structure of the virus rather than with the viral particles. This type of approach might lead to the inhibition of the virus avoiding the occurrence of viral resistance common to most antiviral drugs (*e.g.*, specification page 4).

Stewart also does not disclose Applicants' claimed subject matter and does not make up for Root' s deficiency in that it suffers from the same defects.

Stewart teaches and discloses the anti-cancer activity of resveratrol (*e.g.*, page 13244, col. 1, lines 3-4).

Accordingly, for the reason set forth above, Root and Stewart, alone or in combination, do not disclose the claimed subject matter. Further, it is submitted that there is no motivation to combine their teachings to arrive at the presently claimed invention. Root only provides for a highly specific PKC inhibitor to block the entry mechanism of the influenza virus, while Stewart is completely silent with regard to any antiviral activity of resveratrol. On the contrary, the presently claimed invention, as set forth above, is directed to the unexpected results that resveratrol inhibits only the replication and not the entry of the influenza virus.

Thus, the teaching of Root combined with the teaching of Stewart is not the presently claimed invention.

Heredia also does not teach Applicants' claimed invention and does not correct Root's and Stewart's deficiencies.

As previously submitted, Heredia teaches that resveratrol synergistically inhibits HIV replication (*e.g.*, summary, lines 3-5). Given that the teaching on HIV-1 is non-transferable to influenza, the skilled person would not find the motivation in Heredia for

using resveratrol, which is described as having low antiviral activity and is used to enhance the antiviral activity of specific anti-HIV drugs (*e.g.*, Heredia, abstract). Thus, the combination of Root and Heredia are incompatible.

Moreover, Applicants respectfully disagree with the Examiner's statement that resveratrol is a natural "widely used natural product" indicating that it is already safely used , in vivo, and can be obtained at a low-cost. This statement does not provide the motivation for a skilled artisan to combine the teachings of Root with Stewart. The fact that resveratrol can be used in vivo and that it is low cost is irrelevant with regard to the motivation to combine Root with Stewart. The mere low cost cannot be a sufficient incentive for trying a drug, when activity (see Heredia abstract, 20-30% activity) and safety (see Stewart toxic effects of resveratrol in mammals, page 13249, right col., second paragraph) are the major concerns before starting a treatment.

As set forth above, Root stand for the proposition of inhibiting viral entry into the target cells with a very specific PKC inhibitor. Stewart is completely silent with regard of viruses and only discloses a compound whose very weak PKC inhibition cannot even account for its anti-tumor activity. Heredia teaches an anti-HIV combination. Thus, none of the three references, alone or in combination, teaches using resveratrol to inhibit influenza virus replication and influenza virus treatment. On the contrary, as set forth above, Root and Stewart and Root and Heredia are mutually exclusive with the regard of using resveratrol for its PKC inhibitory activity and with regard of going from HIV to influenza virus, respectively.

Accordingly, for the reasons set forth above, it is respectfully submitted that the combination of the cited references fails to render obvious the subject matter of claims 4-

9 and 13-18. Thus, withdrawal of the rejection of the claims under 35 U.S.C. § 103 (a) over Root in view of Stewart and Heredia is respectfully requested.

Objection to Claims 13 and 16

Claims 13 and 16 have been amended hereinabove to correct a minor typographical error rendering their objection moot.

Conclusion

This response is being filed within the shortened statutory period for response, thus, no fees are believed to be due. If, on the other hand, it is determined that further fees are necessary or any overpayment has been made, the Commissioner is hereby authorized to debit or credit such sum to Deposit Account No. 02-2275.

Pursuant to 37 C.F.R. § 1.136(a), please treat this and any concurrent or future reply in this application that requires a petition for an extension of time of its timely submission as incorporating a petition for extension of time for the appropriate length of time. The fee associated herewith is to be charged to the above-mentioned deposit account.

An early and favorable action on the merits is earnestly solicited.

Respectfully submitted

Date: January 13, 2010

LUCAS & MERCANTI, LLP

By: /Silvia Salvadori/
Silvia Salvadori
Reg. No. 48,265
475 Park Avenue South
New York, NY 10016
Phone: (212) 661-8000
Fax: (212) 661-8002